

REMARKS

Reconsideration of this application is respectfully requested. Claims 1, 11-14, 18-22, 23, and 28 have been amended. Claims 17, 27 and 28 have been cancelled. New claims 29-34 have been added. With these amendments, claims 1, 4-7, 11-15, 18-26, and 28-34 are currently pending in this application. These amendments are made without prejudice or disclaimer and do not add any new matter. Applicants retain the right to prosecute any cancelled or otherwise unclaimed subject matter in a continuing, divisional or other application as appropriate. Consideration and entry of this reply is respectfully requested.

Objection Under 37 C.F.R. 1.75(c)

Claims 11-14 and 23 stand objected to under 37 C.F.R. 1.75(c) as being of improper dependent form for failing to further limit the subject matter of previous claim 1 because the term "tumor antigen" is used instead of "melanoma-associated tumor antigen". Claims 11-14 and 23 have been amended and now refer to a "melanoma-associated tumor antigen". Applicants therefore respectfully request withdrawal of these objections.

Claims 11 and 12 were also objected to for inclusion of RAGE antigens into the list of melanoma-associated antigens. In addition, claims 11 and 12 have been amended to delete reference to RAGE antigens. However, in the event that RAGE antigens are determined to in fact be melanoma-associated antigens, Applicants reserve the right to re-incorporate the term into the claims. Given this amendment, it is respectfully requested that this objection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 18-24 stand rejected under 35 U.S.C. § 112, second paragraph as to the term "IFN α 2b". Claim 1 has been amended to include the term "IFN α 2b". Applicants therefore request withdrawal of this rejection.

Claims 18-24 also stand under 35 U.S.C. § 112, second paragraph as to the term "at least 10 MU/m²/day". The Examiner alleged that the phrase "10 MU/m²/day" is more narrow than "at least 10 MU/m²/day". Claim 1 has been amended to include the

phrase “at least 10 MU/m²/day”. Applicants therefore respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1 and 4-22 stand rejected under 35 U.S.C. § 112, first paragraph as being non-enabling. At page 8 of the Office Action, the Examiner alleges that the specification is not enabled for: 1) any tumor antigen other than a melanoma-associated antigen; 2) “subsequent administration of any interferon other than interferon α 2b”; and, 3) administration of interferon α 2b at any dose for any regimen. Applicants respectfully disagree and traverse these rejections as indicated below.

As to the first allegation, claims 11-14 have been amended to more clearly indicate that the relevant tumor antigens are melanoma-associated tumor antigens. In addition, claims 11 and 12 have been amended to delete reference to RAGE. Applicants respectfully disagree with the Examiner’s apparent allegations that MAGE, BAGE and GAGE are not melanoma-associated antigens. The instant specification points to published documents that clearly demonstrate that MAGE- BAGE, and GAGE are in fact melanoma-associated antigens (see, for example, U.S. Pat. No. 6,235,525; Boel, et al. Immunity, 2: 167-175 (1995) (attached); and, Van den Eynde et al. J. Exp. Med., 182: 689-698 (1995) (attached)). Thus, reference to MAGE, BAGE and GAGE in claims 11 and 12 has been maintained. For these reasons, it is respectfully requested that the rejection, as it relates to these points, is withdrawn.

Regarding the second allegation, claim 1 has been amended to specifically refer to interferon alpha 2b (IFN- α 2b). It is therefore respectfully requested that the rejection, as it relates to the second allegation, is withdrawn.

Finally, the Examiner alleges that the specification is only enabled for a treatment regimen consisting of 20 MU / m² / day for five days per week for four weeks because “in the art at the time of filing, the administration of IFN- α 2b for treatment of melanoma was and has been unpredictable”, citing Sabel et al. (Drugs, 63(11): 1053-58 (2003). As such, “[i]n light of the unpredictabilities...only the dose regiment disclosed in the specification of instant application is considered enabled.” The Examiner also alleged that “[t]here is no enabling support either disclosed in the specification or in the art [for]

'subsequently administering 10 MU/m²/day of interferon alpha'''. The Examiner alleged that Sabel et al. show that "using low-dose and intermediate-dose regimens demonstrated no benefits to survival". The Examiner further alleged that the case law relied upon in Applicants' previous response is inapplicable ("...the subject matter and status of the art of instant application are distinct from the recited case laws.") Thus, the Examiner concluded, the state of the art, the unpredictability thereof, and the lack of specific guidance and working examples in the specification leads to the conclusion that one of skill in the art would be subjected to undue experimentation in practicing the claimed method. Applicants respectfully disagree with this conclusion as indicated below.

The Sabel reference is completely silent as to administration of IFN- α 2b following immunization with a nucleic acid encoding a tumor antigen, as instantly claimed. The only mention of vaccines is at p. 1054, col. 2, last paragraph, which references a comparison trial between a vaccine and high dose IFN- α 2b treatment. The reference does describe variability observed in the effectiveness of IFN- α 2b treatment in various clinical trials. Applicants disagree that this variability in any way renders the instantly claimed method non-enabled.

The Examiner alleged that the "subject matter and status of the art of the instant application are distinct from the recited case laws." Applicants maintain that while the facts may be distinct, the principles are the same. That the specific technologies differ from those of Genentech, Amgen, and Soll, is not dispositive of the applicability of principles set forth in those cases to the instant situation. The enablement requirement is satisfied if teaches one of skill in the art to make and use the invention without "undue experimentation." Genentech v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed.Cir.1997); In re Vaeck, 947 F.2d 488, 495. A patentee need only "provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims." Amgen v. Chugai and Genetics Institute, 927 F.2d 1200, 1213 (Fed. Cir. 1991). Applicants disclosure is in compliance with these requirements, even in view of the variability reviewed by Sabel et al.

Applicants disclosed that administration of high-dose IFN- α 2b following immunization against a tumor antigen results in an effective anti-tumor response. As previously explained, the instantly exemplified starting dosage, 20 MU/m²/day for five

days per week for four weeks, was adjusted downward to alleviate the observed toxic effects of the 20 MU/m²/day initial dosage. For example, paragraph [0083] suggests reducing the dosage by one-third the original dosage (e.g., by about 6.66 MU) twice if necessary due to toxicity. Accordingly, Applicants demonstrated that a 20 MU/m²/day dose, followed in certain cases by a first one-third reduction in dosage, followed in certain cases by a second one-third reduction in dosage (e.g., from the original dosage), was effective. Thus, following the initial 20 MU dosage, a range of from approximately 6-20 MU/m²/day was administered in subsequent administrations. While some amount of professional judgment may be required of the skilled artisan to select the appropriate dosages, the level of skill in the art is extremely high (e.g., a well-trained physician). Applicants have provided a range of dosages from which the skilled artisan may choose to treat a patient (e.g., the examples are not so limited that there is not an adequate basis of support for the amended claims, In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938)). It is simply incorrect that the skilled artisan would be subjected to undue experimentation by beginning treatment at 10 MU/m²/day. One would simply administer the selected dosage and monitor the anti-tumor antigen immune response exhibited by the patient. If no response is observed, the skilled artisan may merely choose to administer a higher dose, and once again monitor the anti-tumor antigen immune response. Similarly, if toxicity is observed, the dosage may simply be lowered (e.g., by one-third as in the Examples). None of these activities would require undue experimentation and are routinely undertaken by those of skill in the art. Applicants believe they have exemplified an acceptable range of doses that legally enables one of skill in the art to practice the claimed methodology (see, e.g., Amgen v. Chugai and Genetics Institute, 927 F.2d 1200, 1213 (Fed. Cir. 1991)). The results of the various doses may not be entirely predictable, but absolute predictability is not required. The burden placed upon the skilled artisan in selecting appropriate dosages is not undue, but simply routine. It is therefore respectfully requested that the rejection, as it relates to this final allegation, be withdrawn.

CONCLUSIONS

Reconsideration of this application is respectfully requested. Applicants believe the claims are in condition for allowance and respectfully request the issuance of a Notice of Allowance as soon as possible. The Examiner is encouraged to contact the undersigned if it is believe doing so would expedite prosecution of this application.

Respectfully submitted,

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